Figure 1

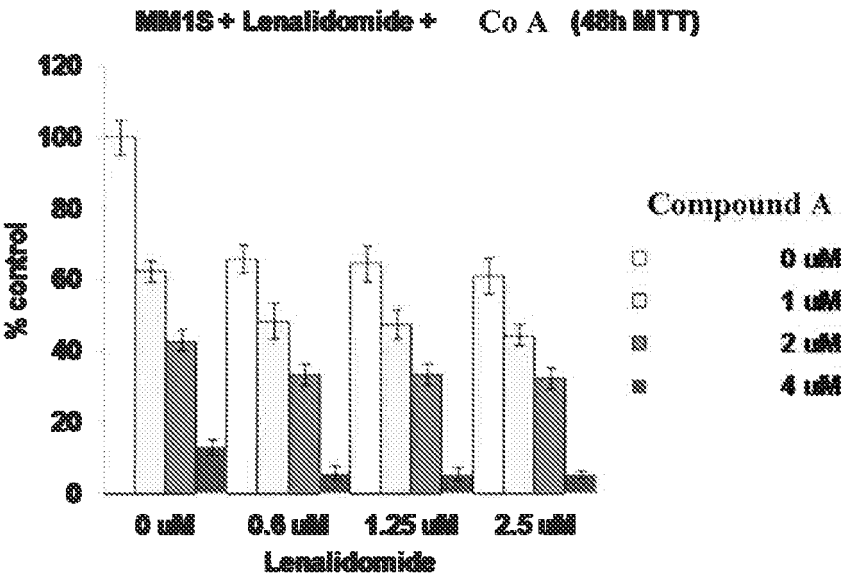


Figure 2

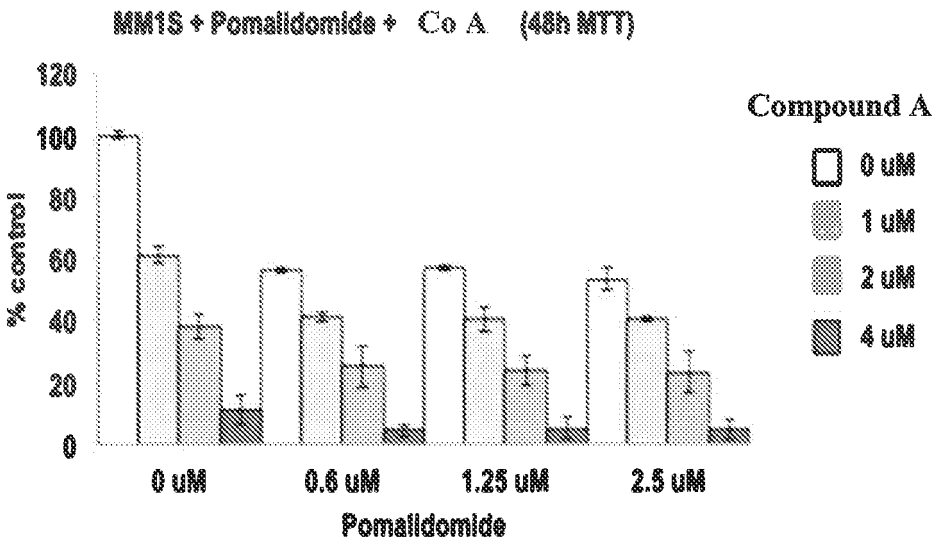


Figure 3

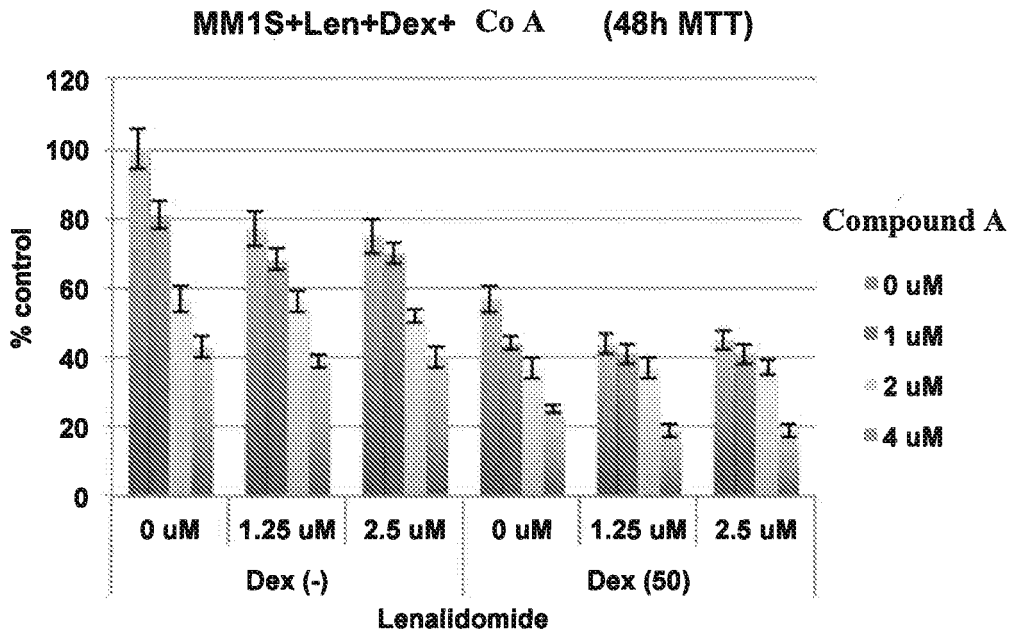
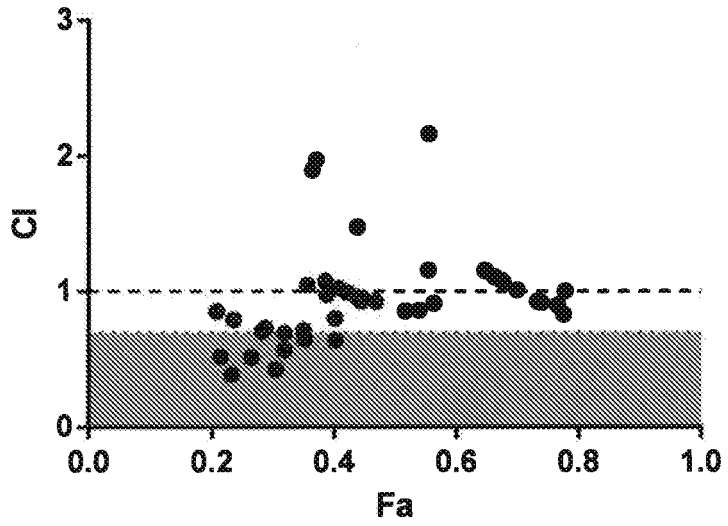

MM1S+Len+Dex+ Co A (48h MTT)
120
100
80
60
40
20
0
% control
Compound A
0 uM
1 uM
2 uM
4 uM
0 uM
1.25 uM
2.5 uM
0 uM
1.25 uM
2.5 uM
Dex (-)
Dex (50)
Lenalidomide

Figure 4A

Compound A + lenalidomide



Compound A + pomalidomide

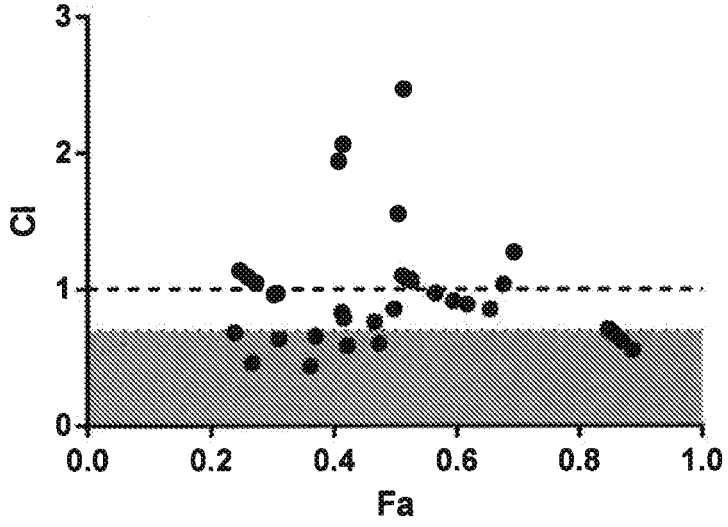
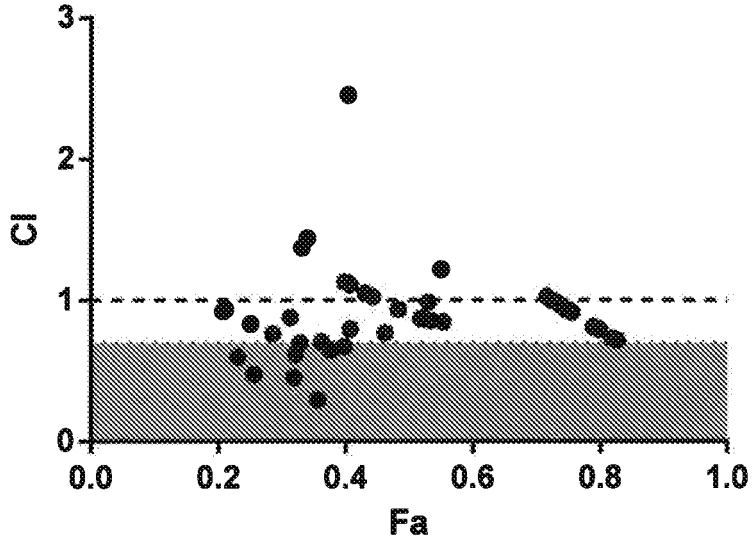


Figure 4B

Compound B + lenalidomide



Compound B + pomalidomide

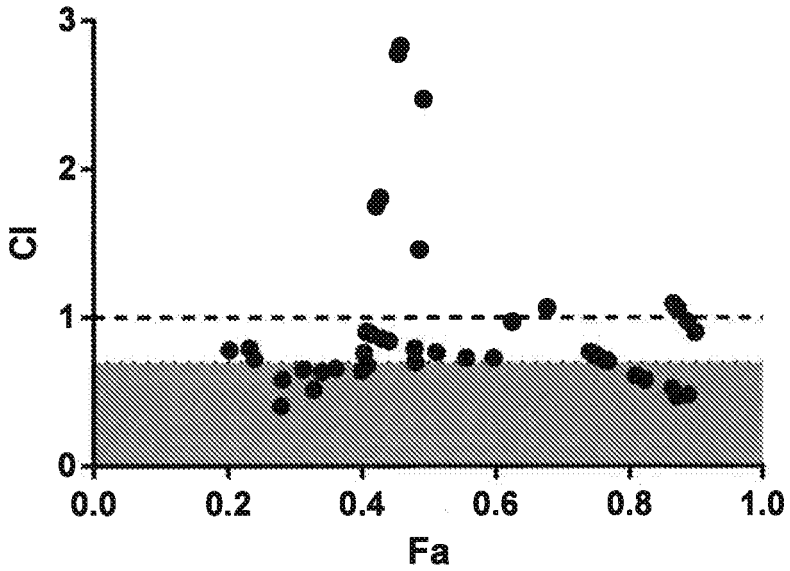
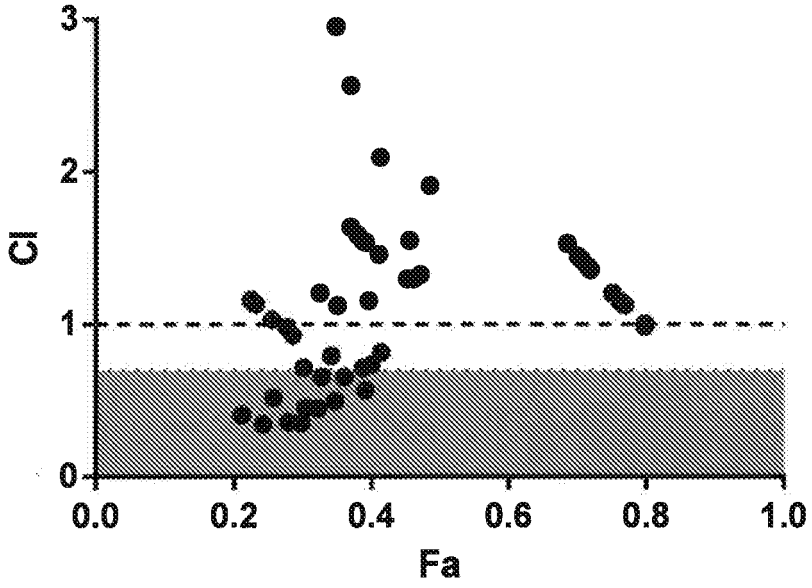


Figure 4C

Compound C + lenalidomide



Compound C + pomalidomide

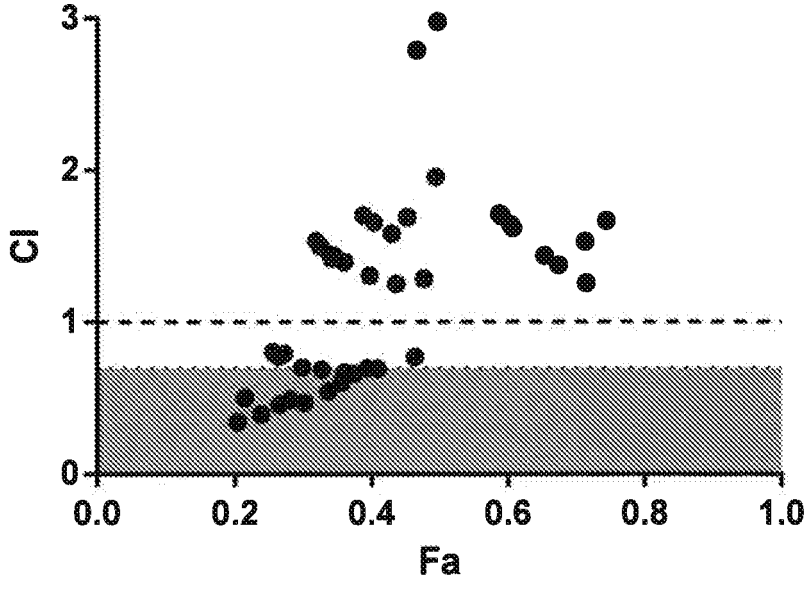
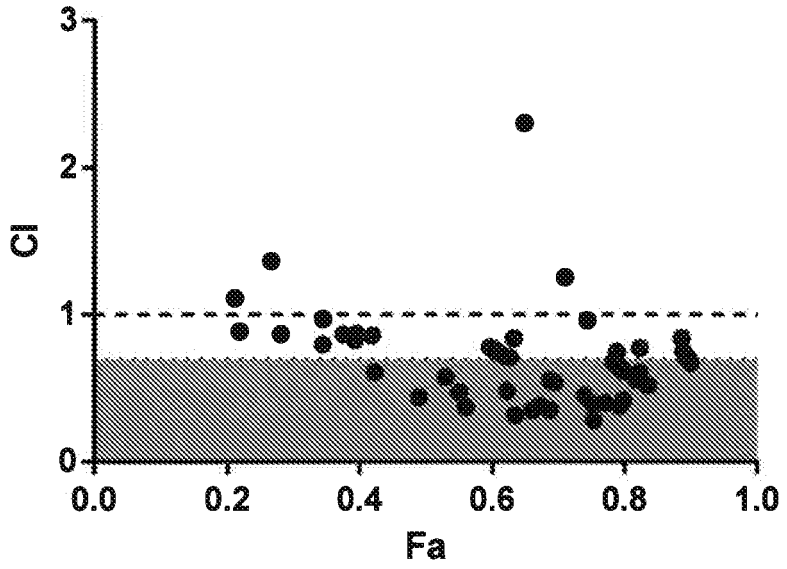


Figure 5A

Compound A + lenalidomide



Compound A + pomalidomide

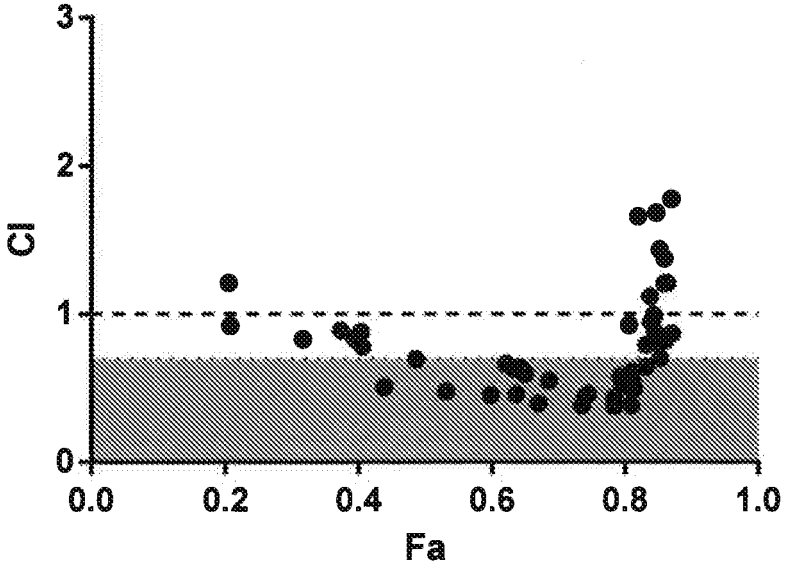
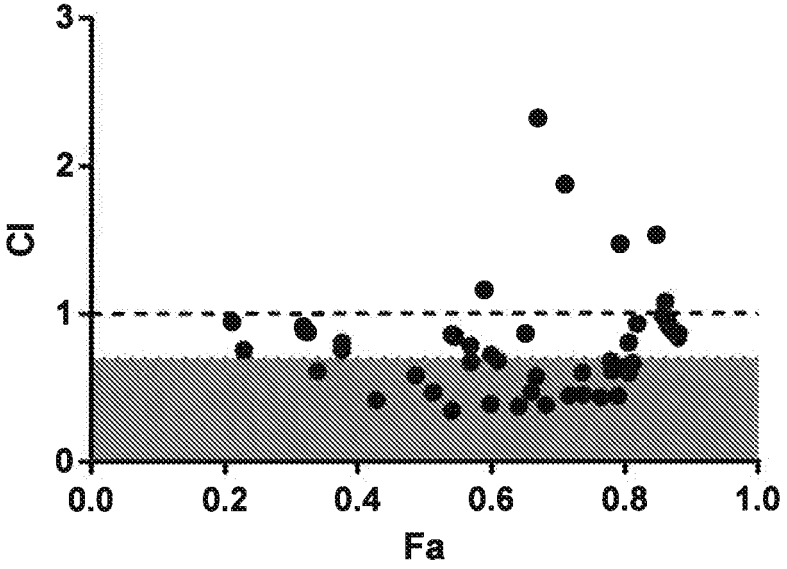


Figure 5B

Compound B + lenalidomide



Compound B + pomalidomide

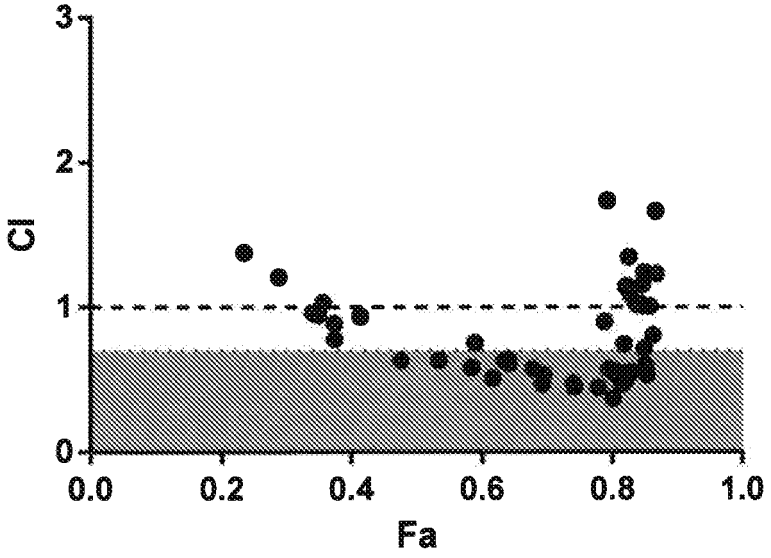
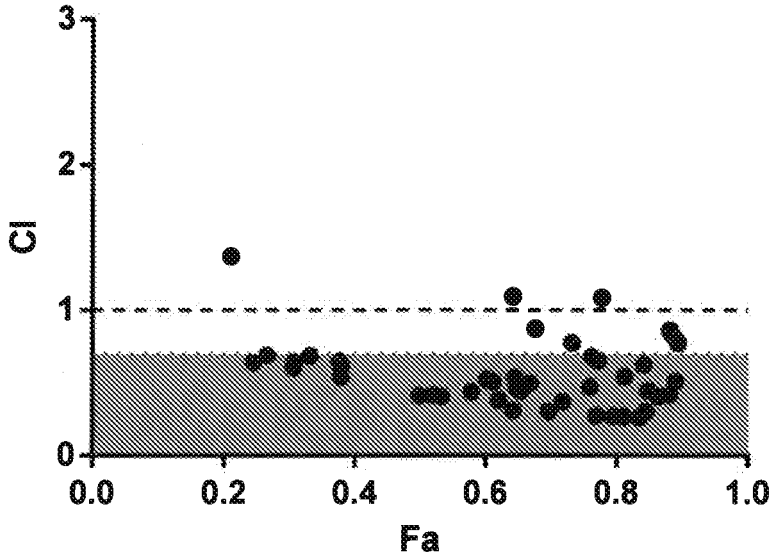


Figure 5C

Compound C + lenalidomide



Compound C + pomalidomide

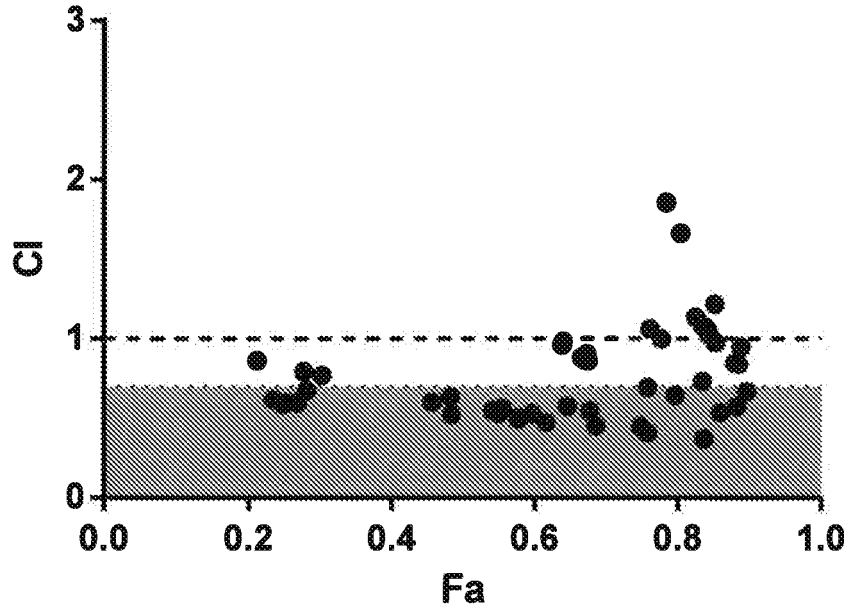
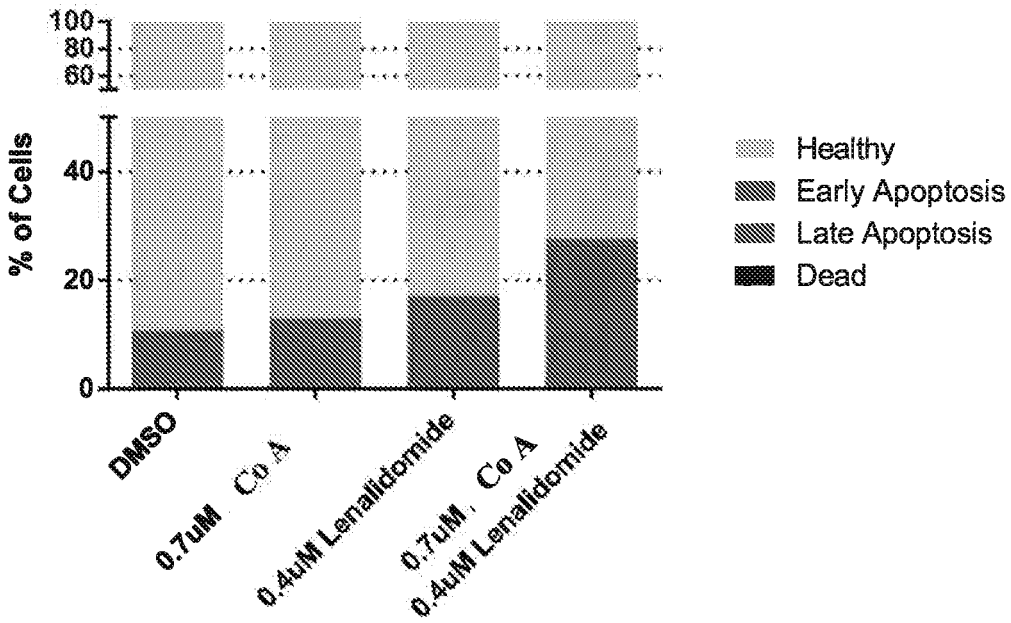


Figure 6

A


100
80
60
40
20
0
% of Cells
Healthy
Early Apoptosis
Late Apoptosis
Dead
DMSO
0.7uM Co A
0.4uM Lenalidomide
0.7uM Co A
0.4uM Lenalidomide

B

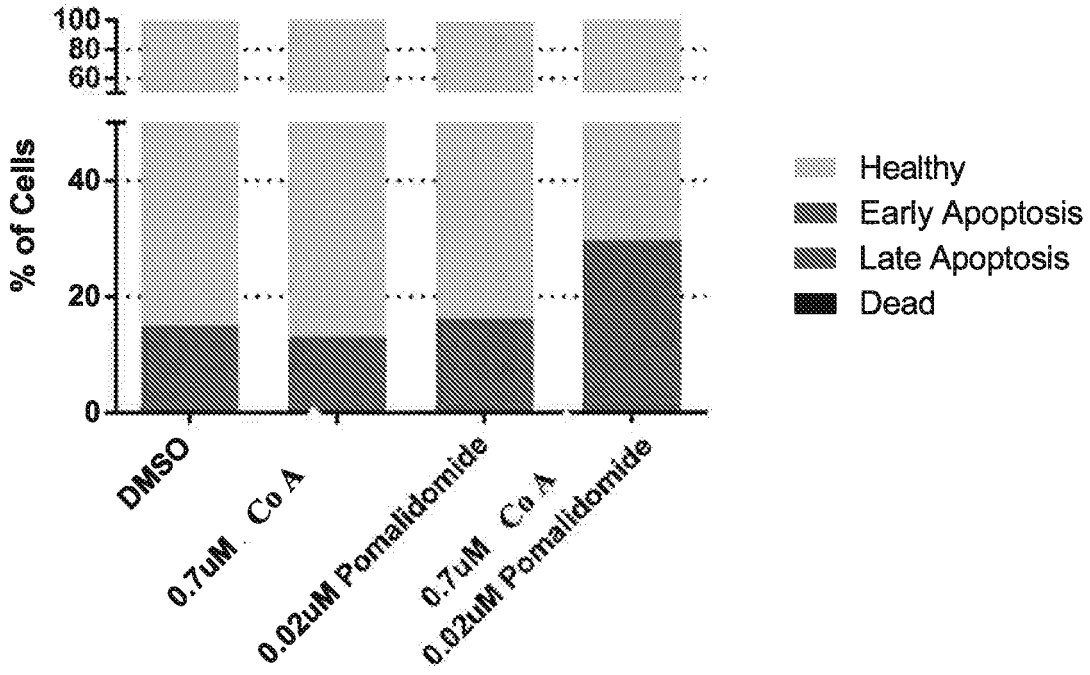
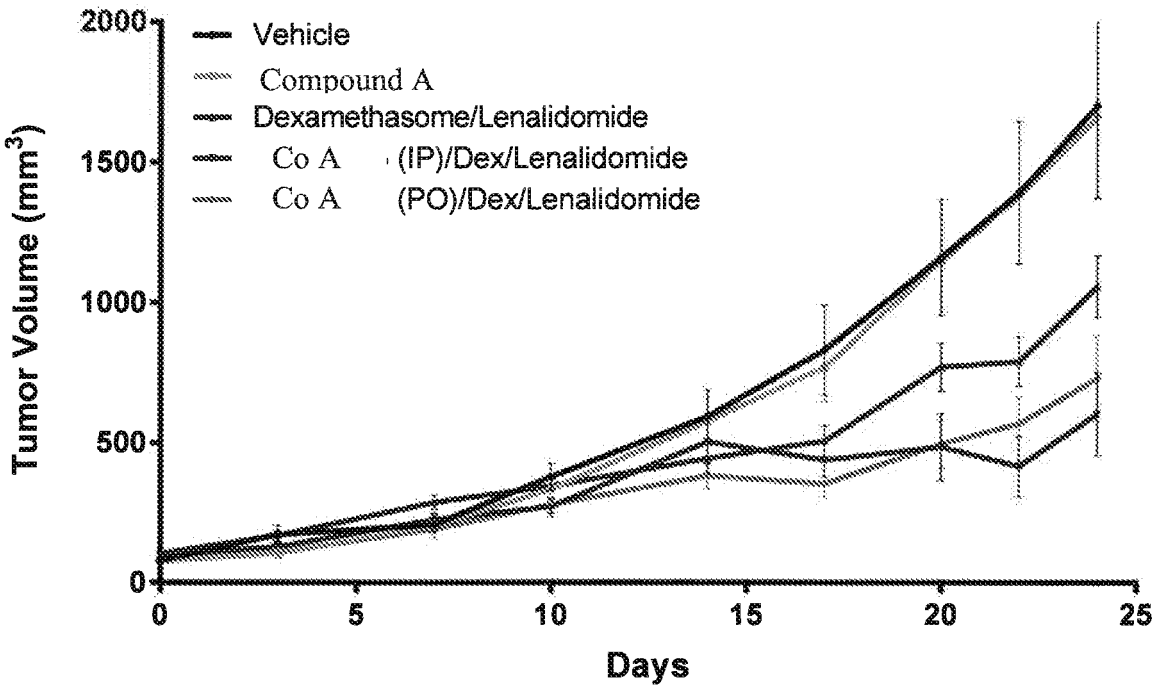

100
80
60
40
20
0
% of Cells
Healthy
Early Apoptosis
Late Apoptosis
Dead
DMSO
0.7uM Co A
0.02uM Pomalidomide
0.7uM Co A
0.02uM Pomalidomide

Figure 7

A


Vehicle
Compound A
Dexamethasome/Lenalidomide
Co A (IP)/Dex/Lenalidomide
Co A (PO)/Dex/Lenalidomide
Tumor Volume (mm3)
2000
1500
1000
500
0
0
5
10
15
20
25
Days

B

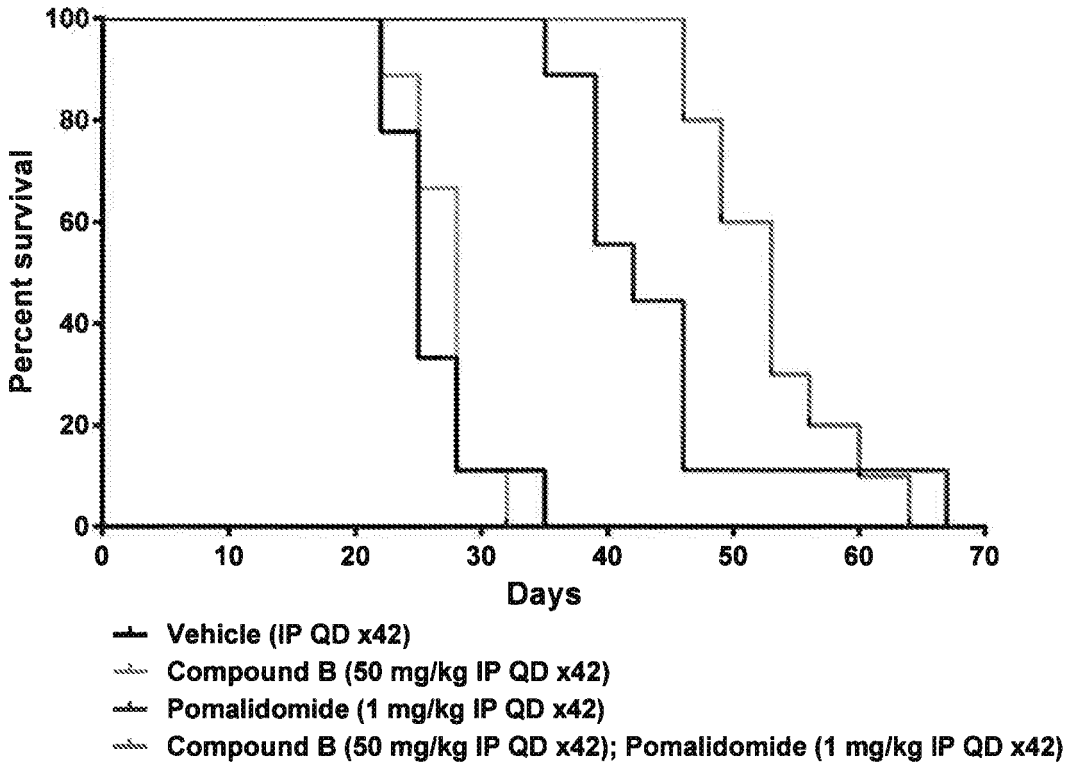
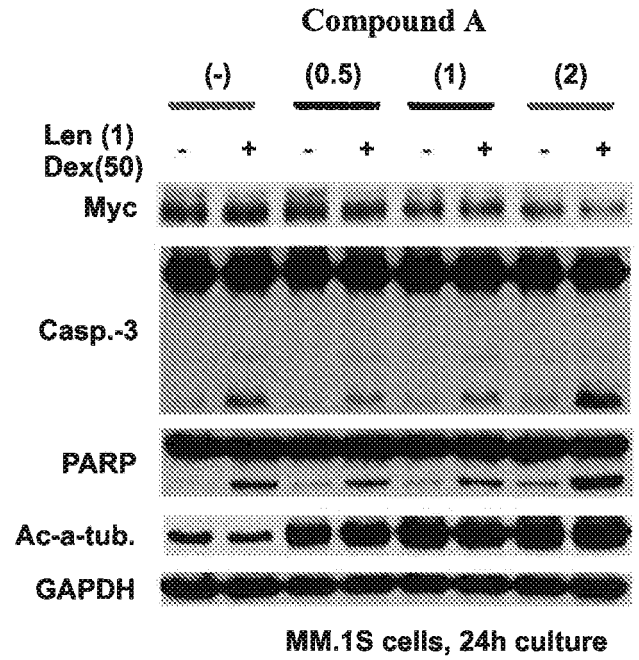
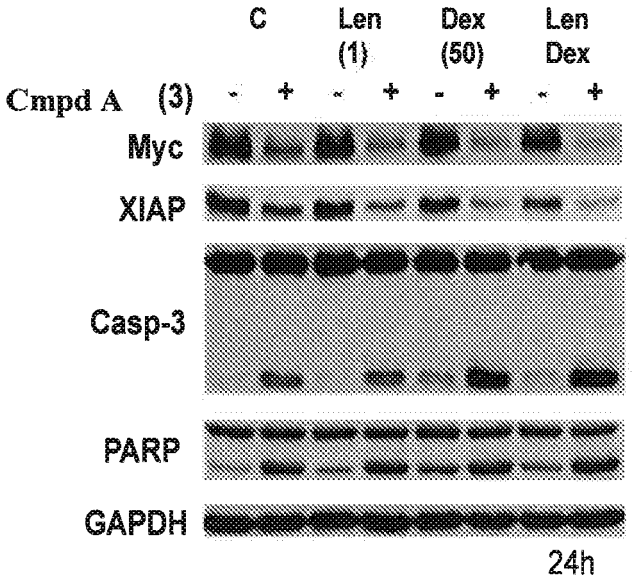

Percent survival
100
80
60
40
20
0
0
10
20
30
40
50
60
70
Days
Vehicle (IP QD x42)
Compound B (50 mg/kg IP QD x42)
Pomalidomide (1 mg/kg IP QD x42)
Compound B (50 mg/kg IP QD x42); Pomalidomide (1 mg/kg IP QD x42)

Figure 8

A


Compound A
(-)
(0.5)
(1)
(2)
Len (1)
Dex(50)
- + - + - + - +
Myc
Casp.-3
PARP
Ac-a-tub.
GAPDH
MM.1S cells, 24h culture

B


C
Len (1)
Dex (50)
Len Dex
Cmpd A (3)
- + - + - + - +
Myc
XIAP
Casp-3
PARP
GAPDH
24h

C

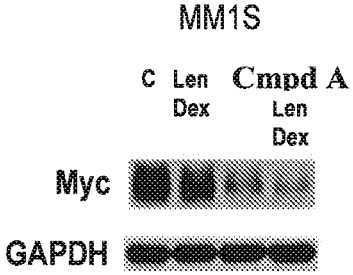

MM1S
C
Len
Dex
Cmpd A
Len
Dex
Myc
GAPDH

Figure 8 (cont.)

D

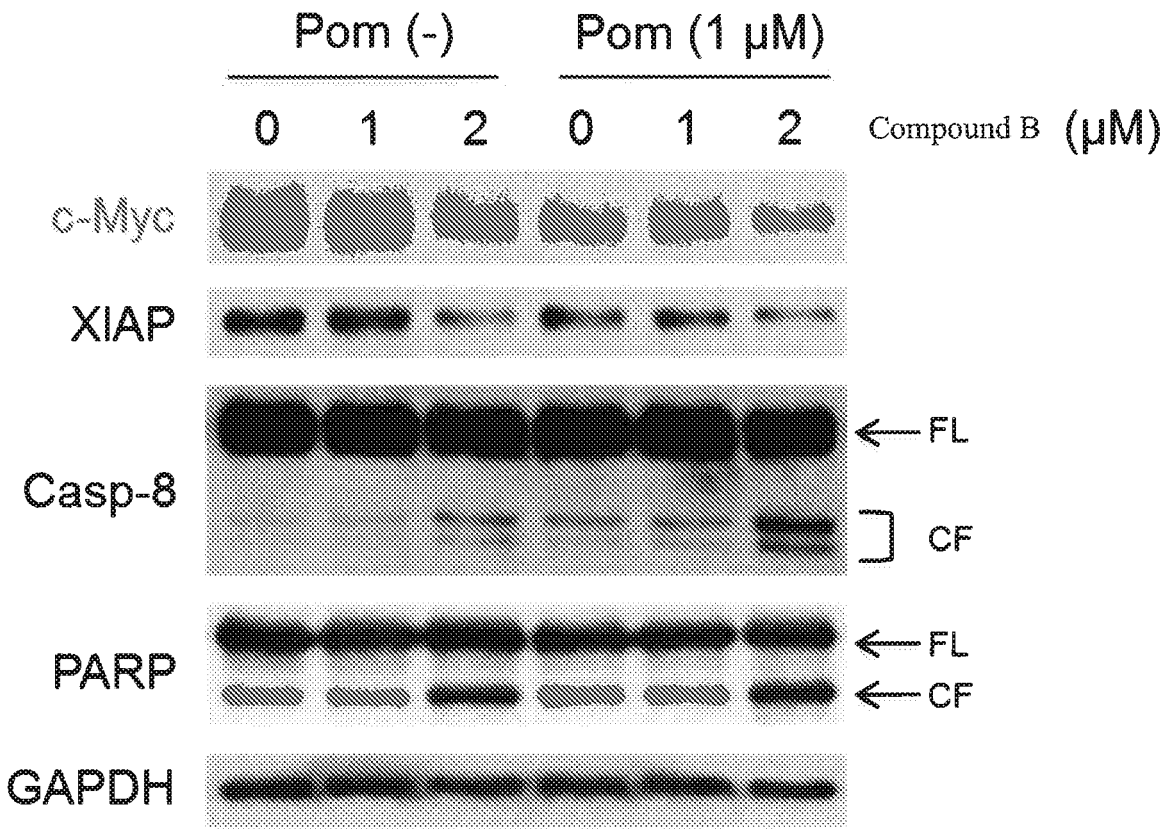
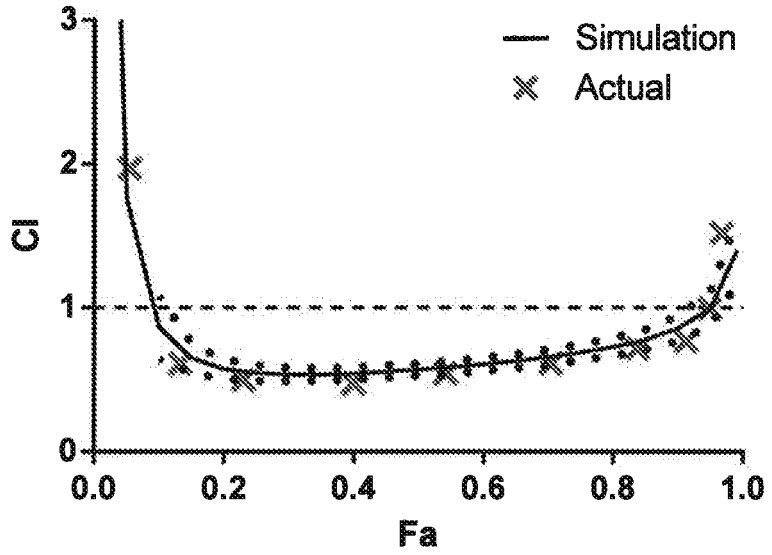


Figure 9A

Compound A + Lenalidomide



Compound A + Pomalidomide

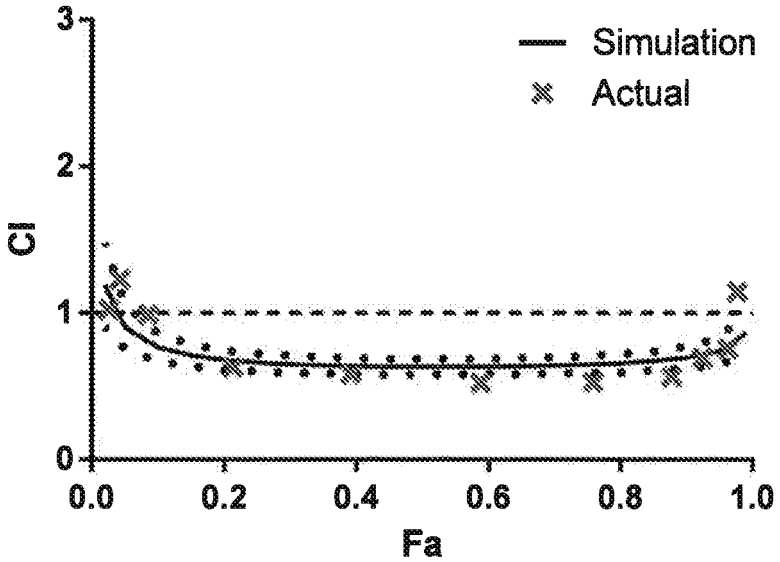
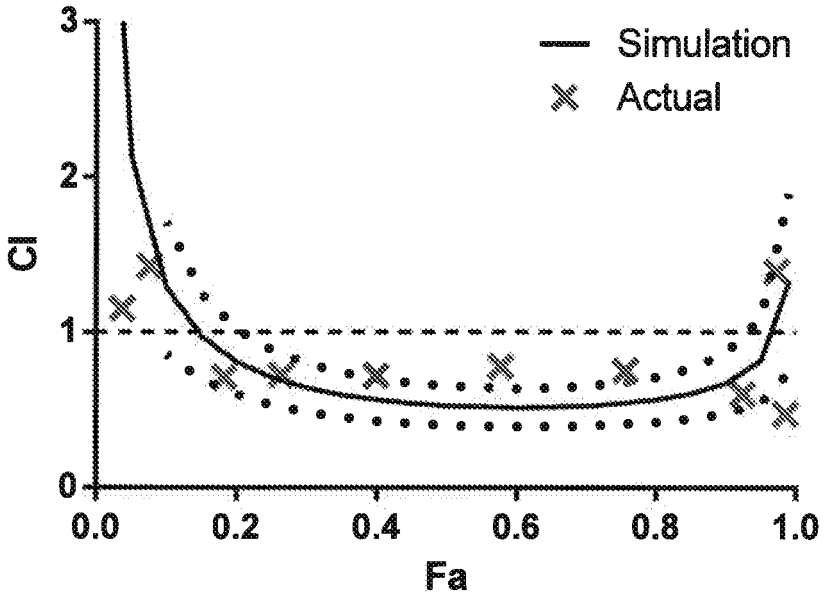


Figure 9B

Compound C + Lenalidomide



Compound C + Pomalidomide

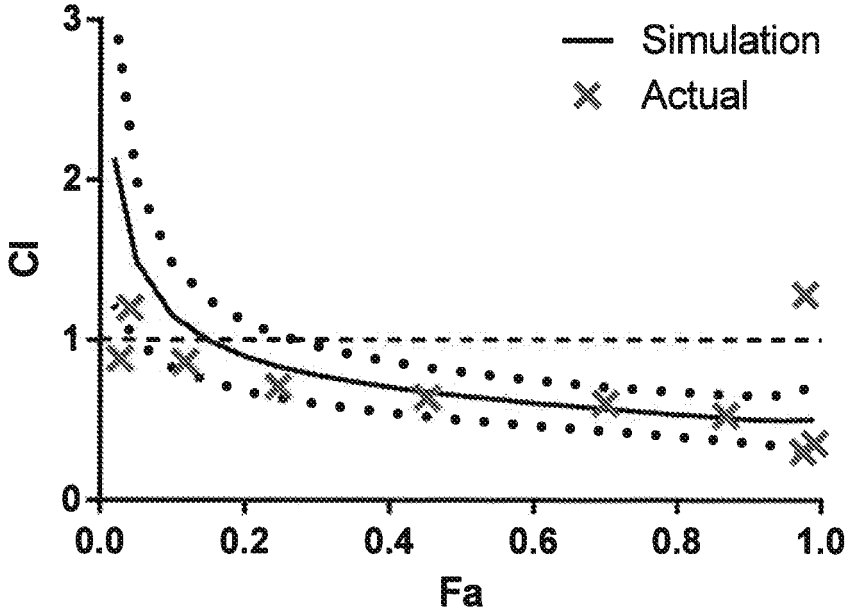
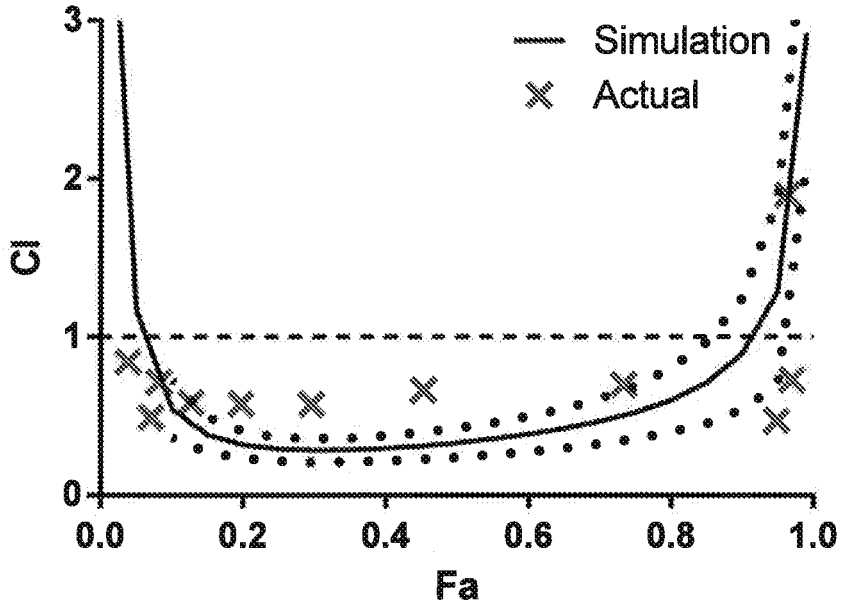


Figure 9C

Compound A + Lenalidomide



Compound A + Pomalidomide

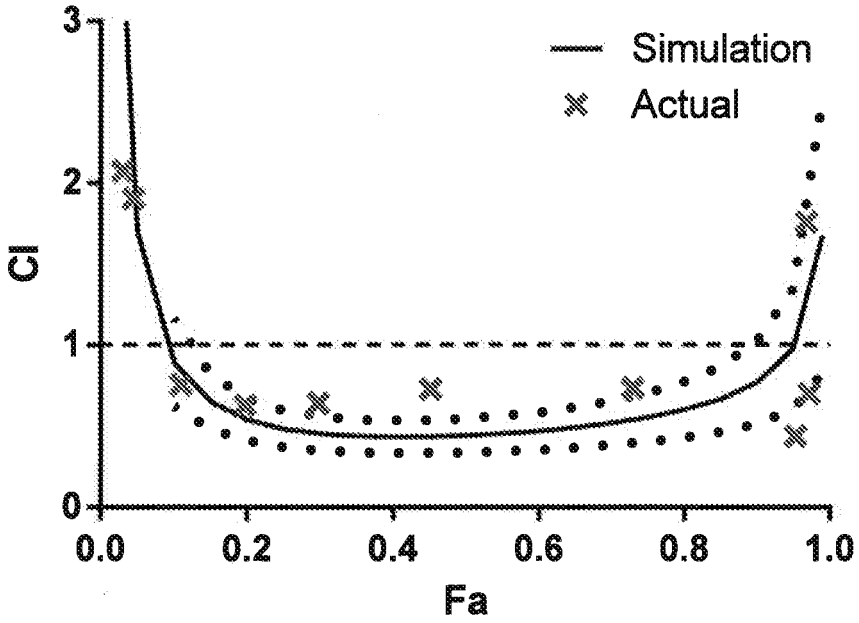
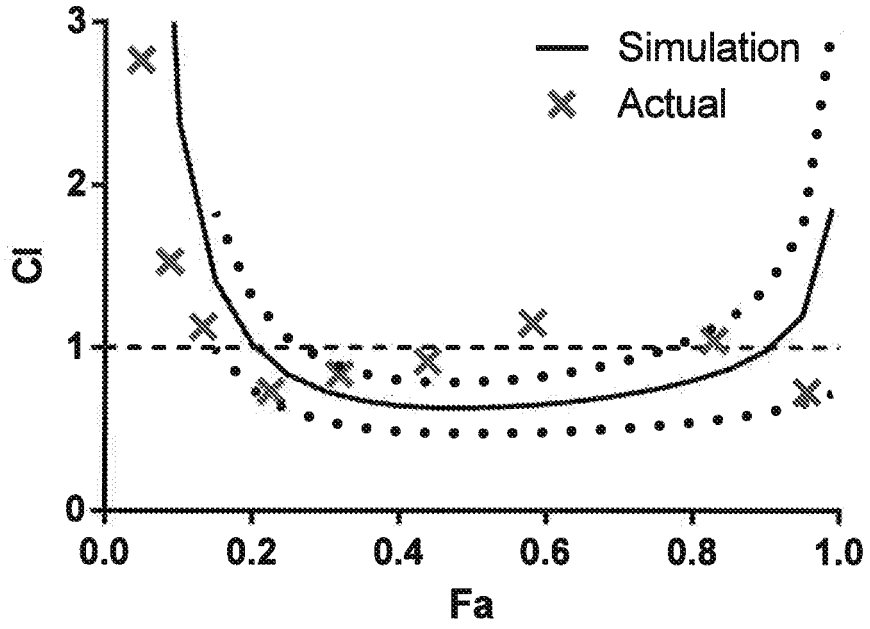


Figure 9D

Compound C + Lenalidomide



Compound C + Pomalidomide

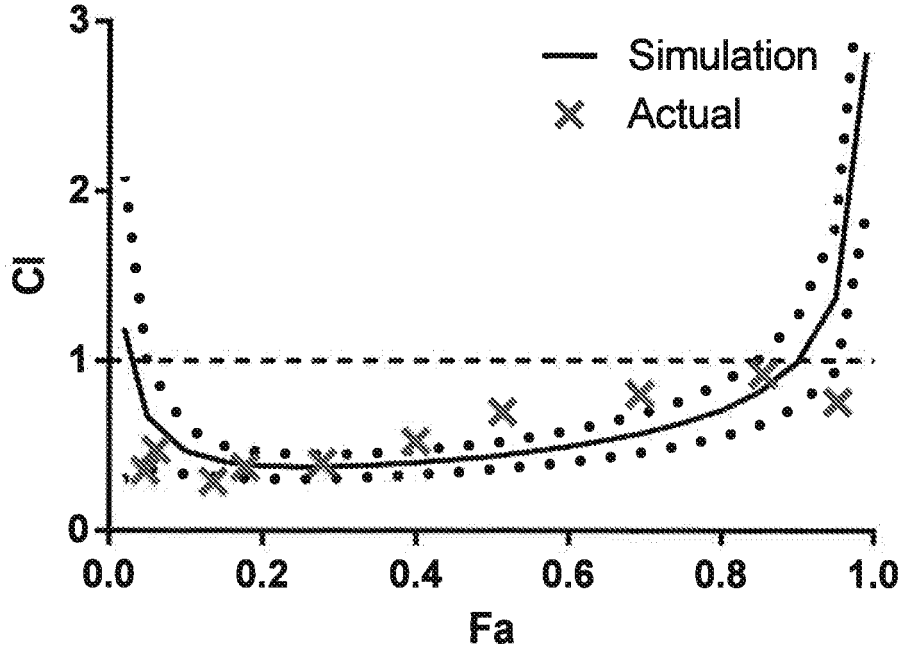


Figure 9E

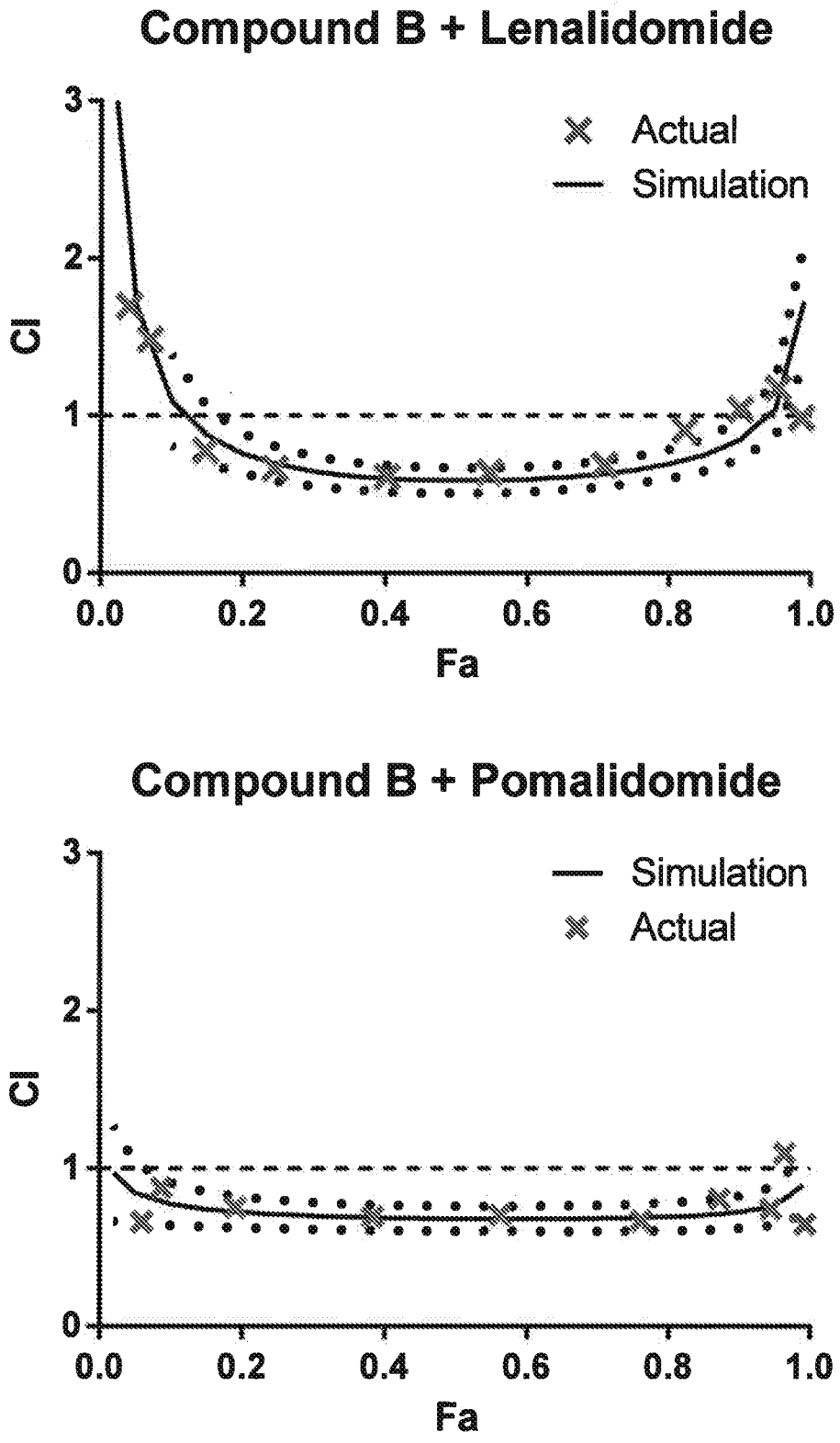
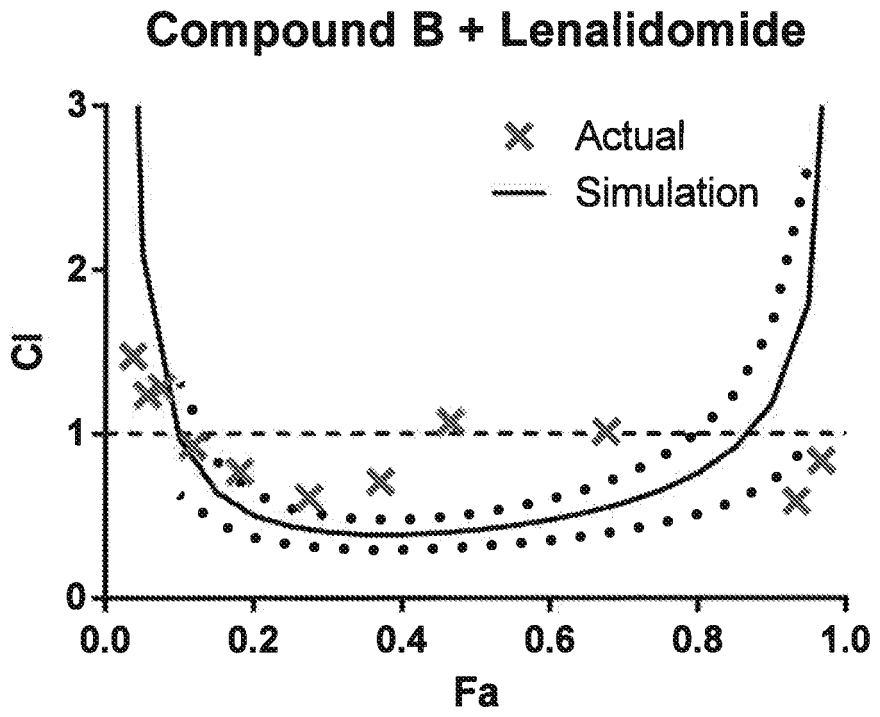

Compound B + Lenalidomide
Actual
Simulation
CI
3
2
1
0
0.0
0.2
0.4
0.6
0.8
1.0
Fa
Compound B + Pomalidomide
Simulation
Actual
CI
3
2
1
0
0.0
0.2
0.4
0.6
0.8
1.0
Fa

Figure 9F


Compound B + Lenalidomide
Actual
Simulation
CI
Fa
0
1
2
3
0.0
0.2
0.4
0.6
0.8
1.0

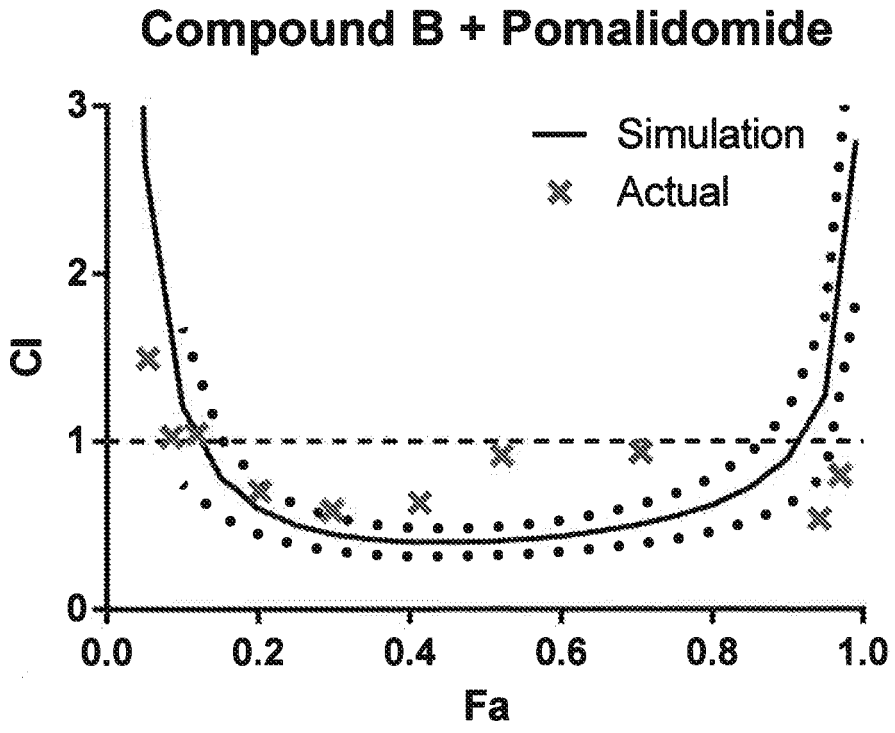
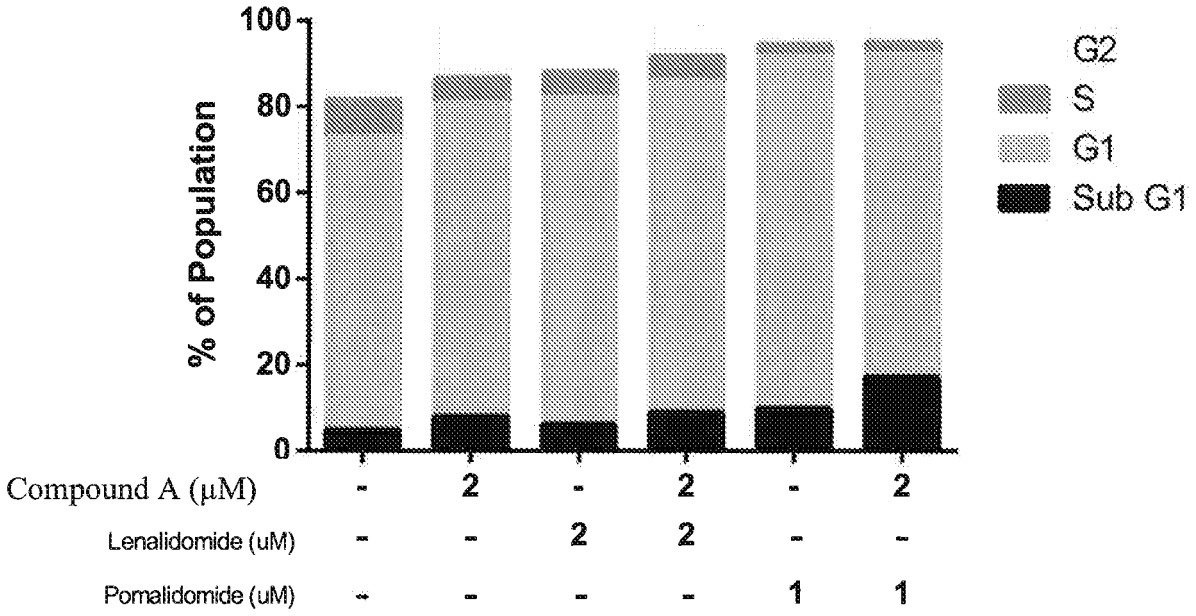

Compound B + Pomalidomide
Simulation
Actual
CI
Fa
0
1
2
3
0.0
0.2
0.4
0.6
0.8
1.0

Figure 10

A


100
80
60
40
20
0
% of Population
G2
S
G1
Sub G1
Compound A (μM) - 2 - 2 - 2
Lenalidomide (uM) - - 2 2 - -
Pomalidomide (uM) - - - - 1 1

B

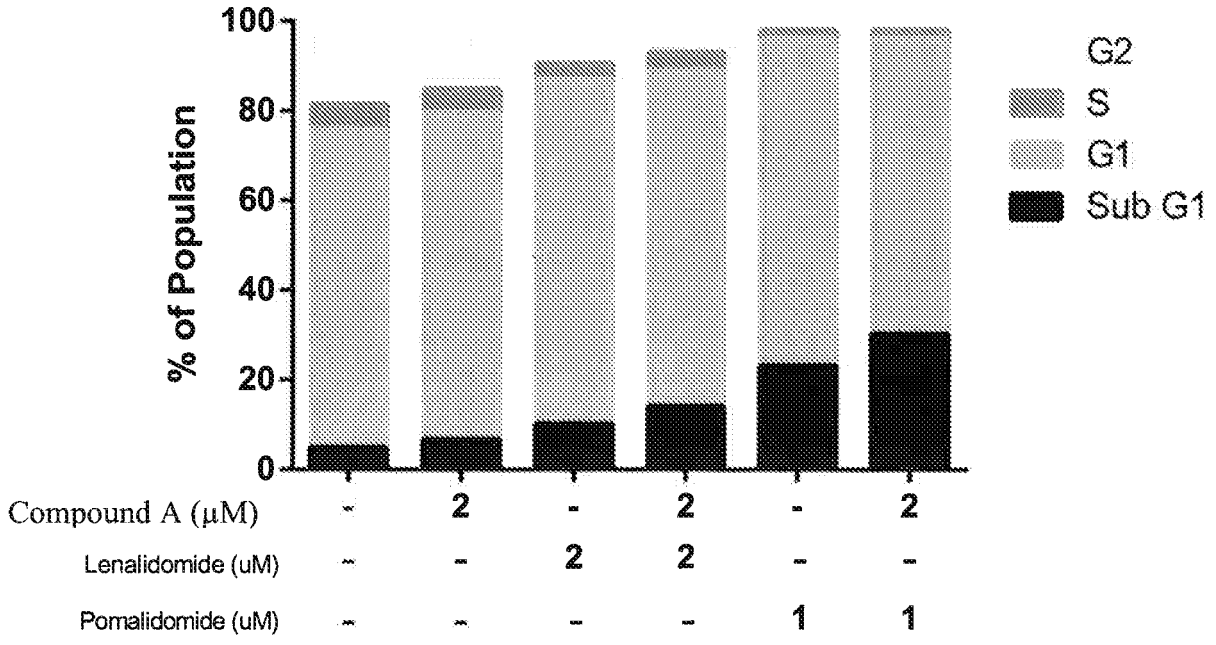
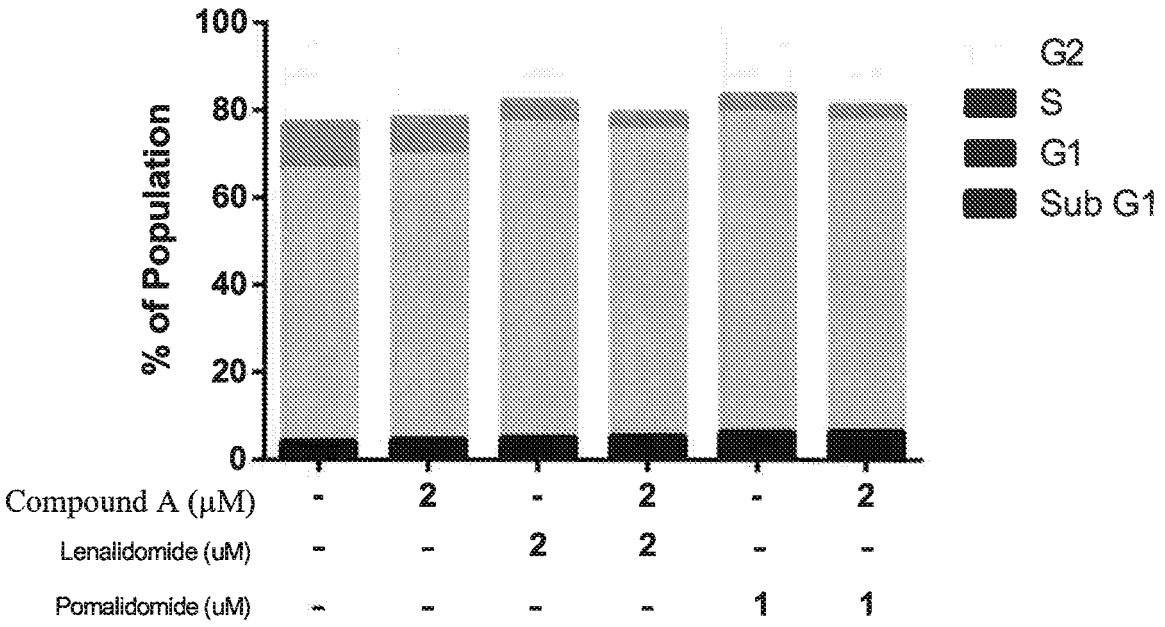

100
80
60
40
20
0
% of Population
G2
S
G1
Sub G1
Compound A (μM) - 2 - 2 - 2
Lenalidomide (uM) - - 2 2 - -
Pomalidomide (uM) - - - - 1 1

Figure 10 (cont.)

C



D

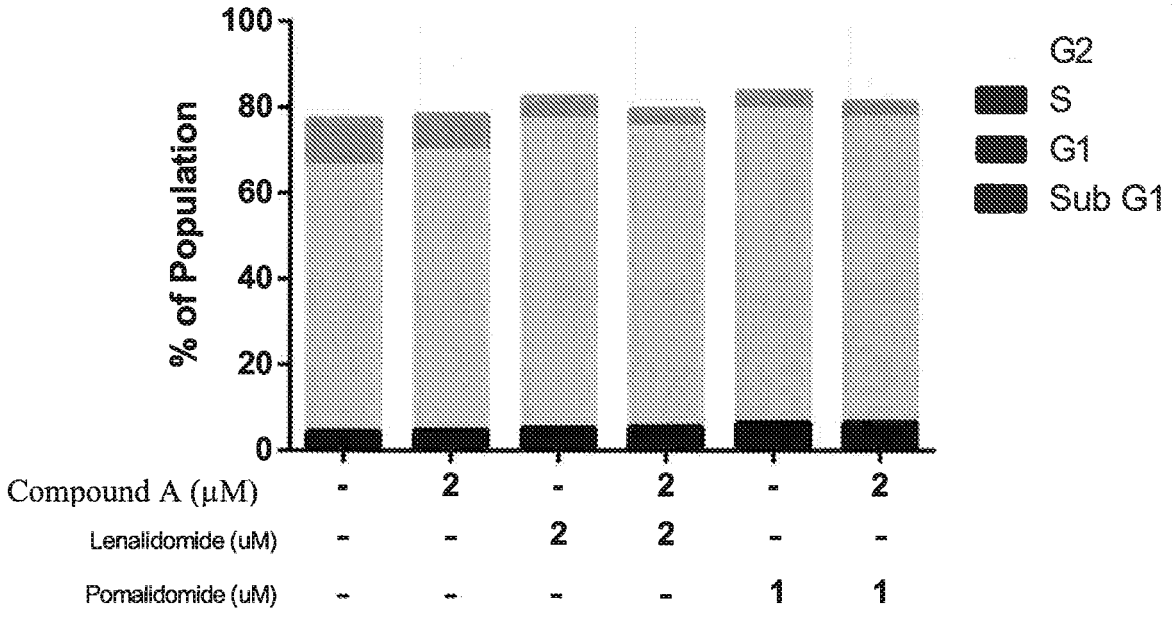
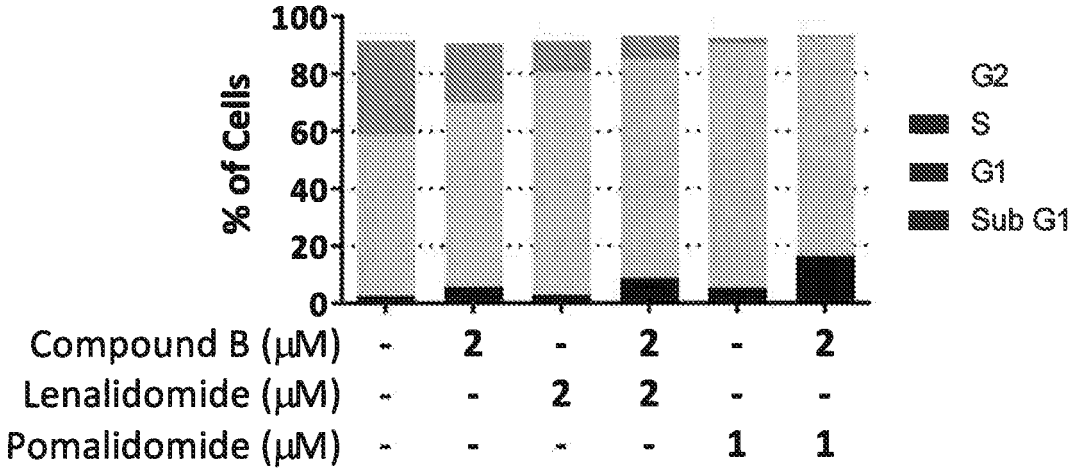


Figure 10 (cont.)

E



F

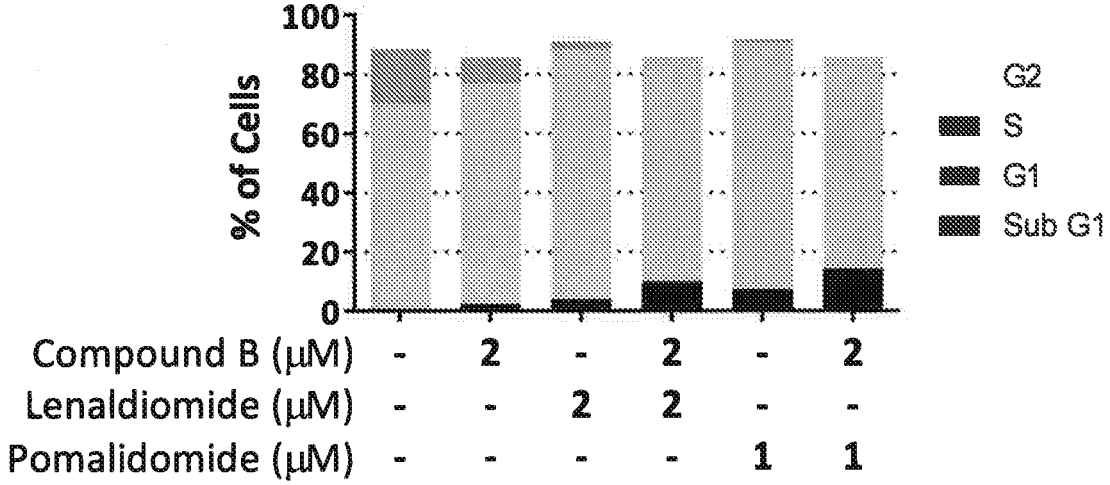
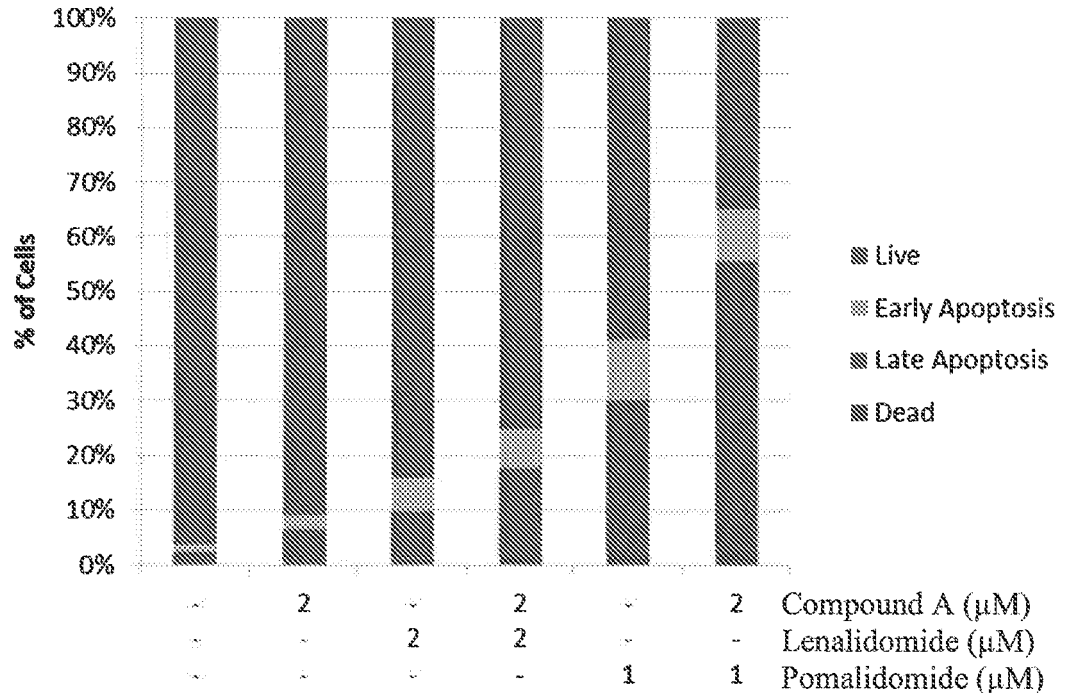


Figure 11

A


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
% of Cells
Live
Early Apoptosis
Late Apoptosis
Dead
- 2 - 2 - 2 Compound A (μM)
- - 2 2 - - Lenalidomide (μM)
- - - - 1 1 Pomalidomide (μM)

B

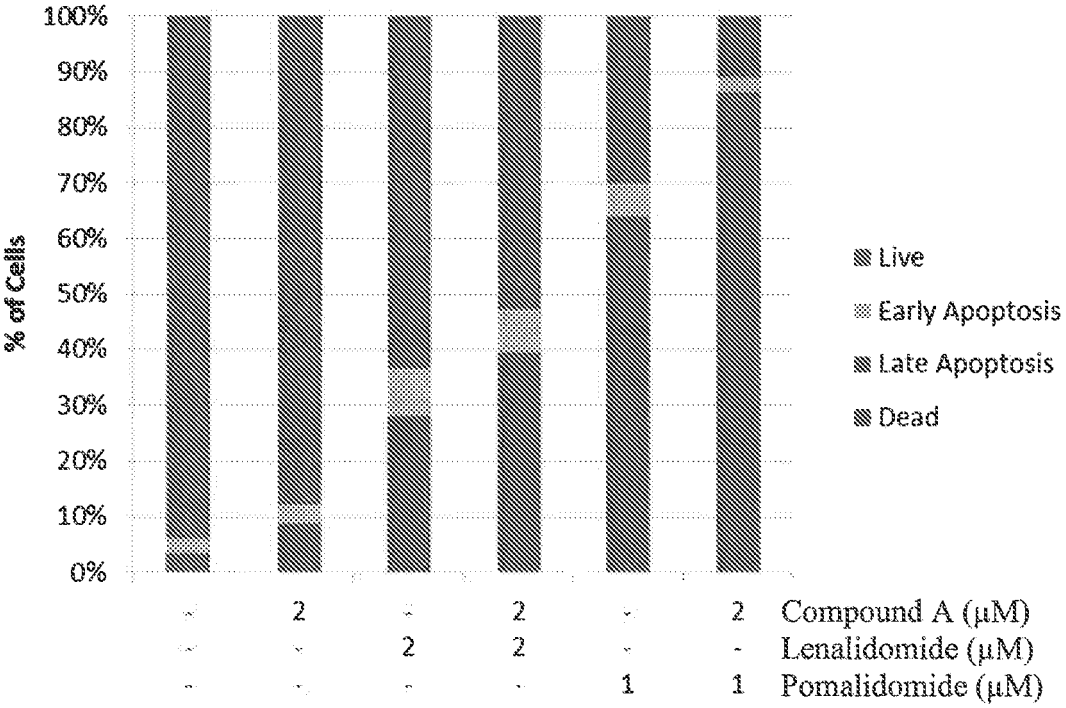
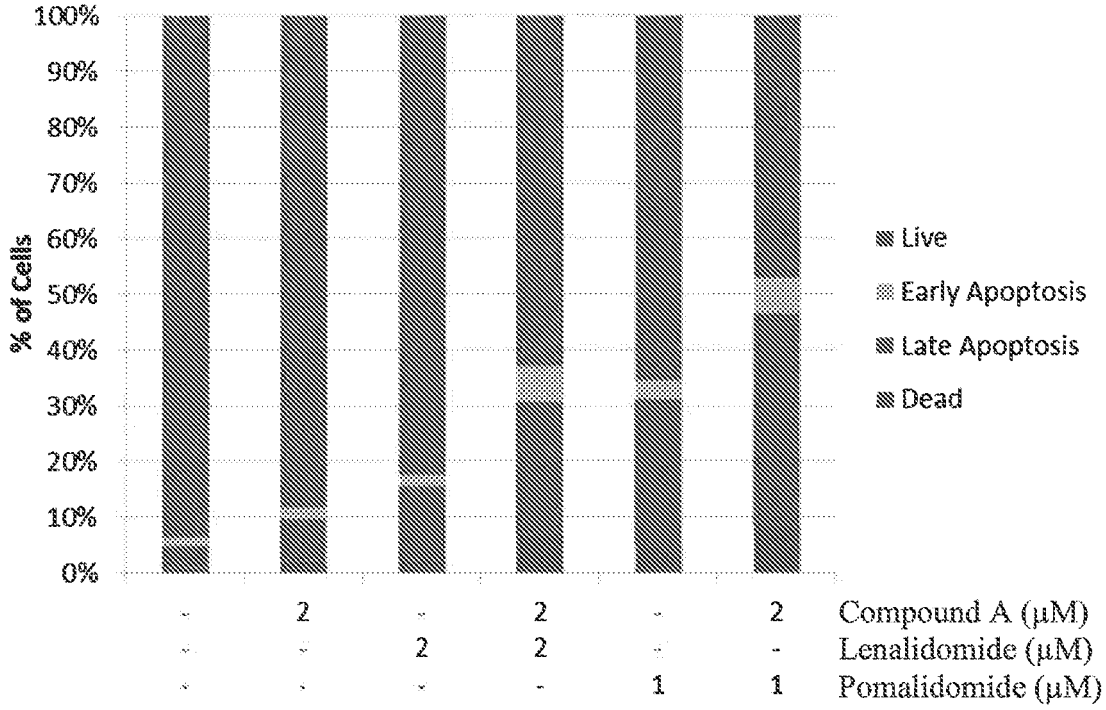

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
% of Cells
Live
Early Apoptosis
Late Apoptosis
Dead
- 2 - 2 - 2 Compound A (μM)
- - 2 2 - - Lenalidomide (μM)
- - - - 1 1 Pomalidomide (μM)

Figure 11 (cont.)

C



D

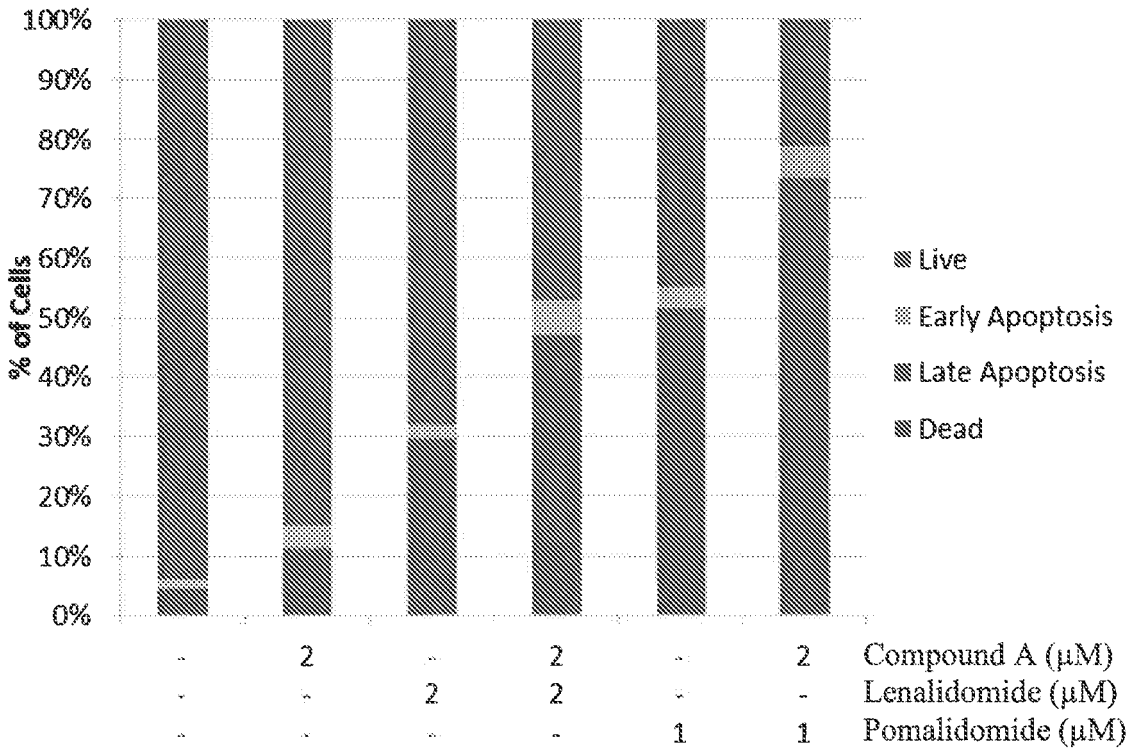
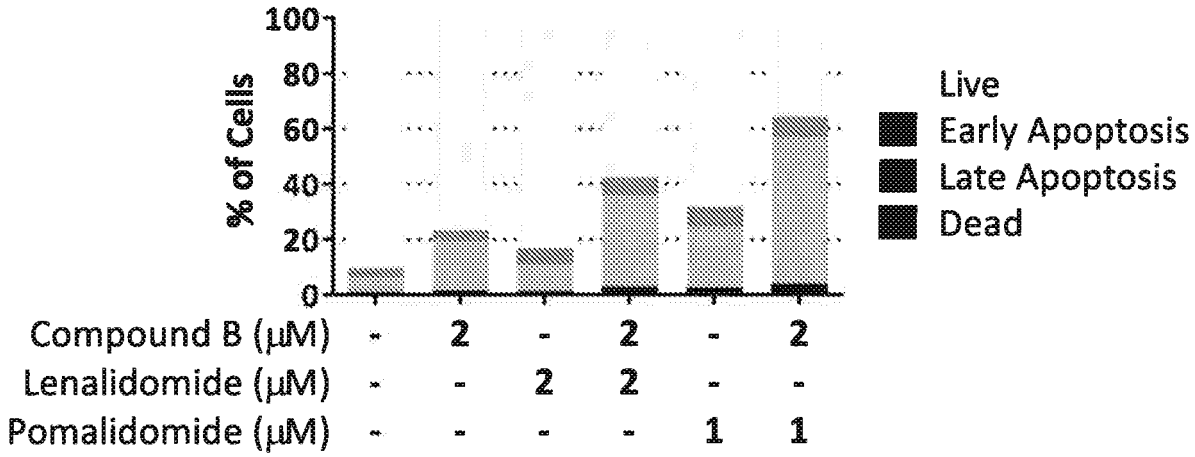


Figure 11 (cont.)

E



F

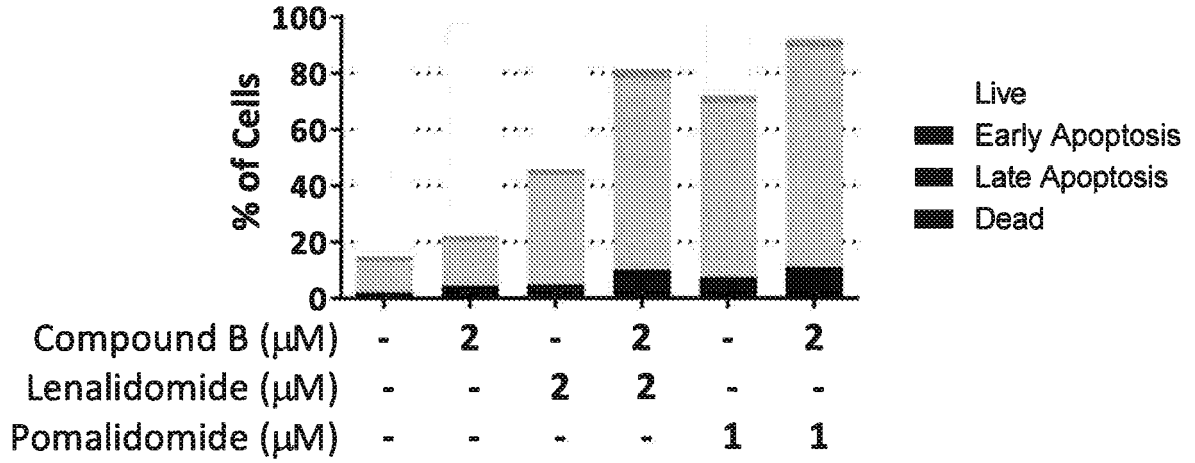
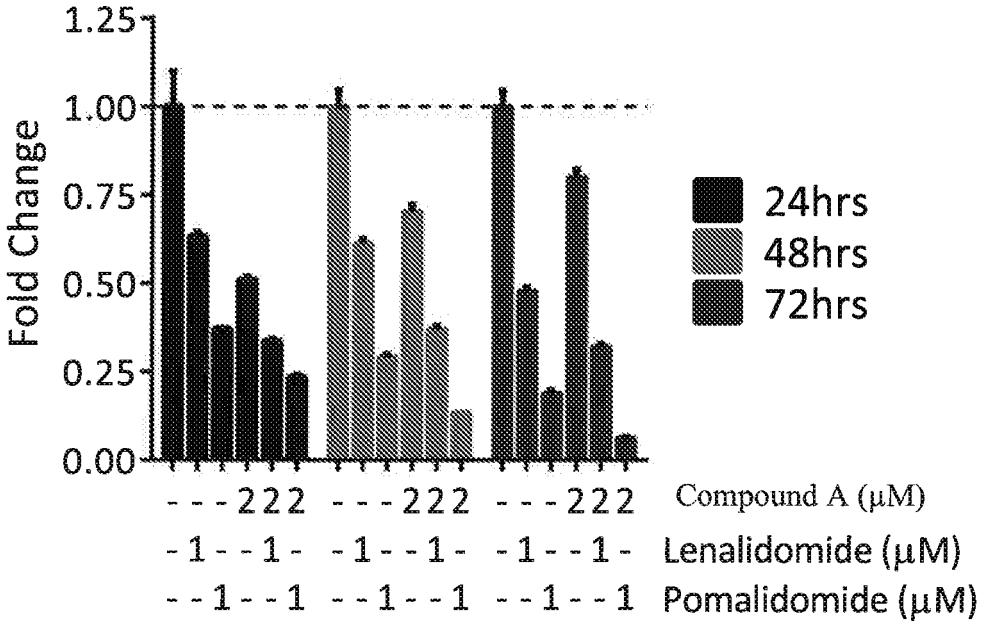


Figure 12

A


1.25
1.00
0.75
0.50
0.25
0.00
Fold Change
24hrs
48hrs
72hrs
- - - 2 2 2 - - - 2 2 2 - - - 2 2 2 Compound A (μM)
- 1 - - 1 - - 1 - - 1 - - 1 - - 1 - - 1 - Lenalidomide (μM)
- - 1 - - 1 - - 1 - - 1 - - 1 - - 1 - - 1 Pomalidomide (μM)

B

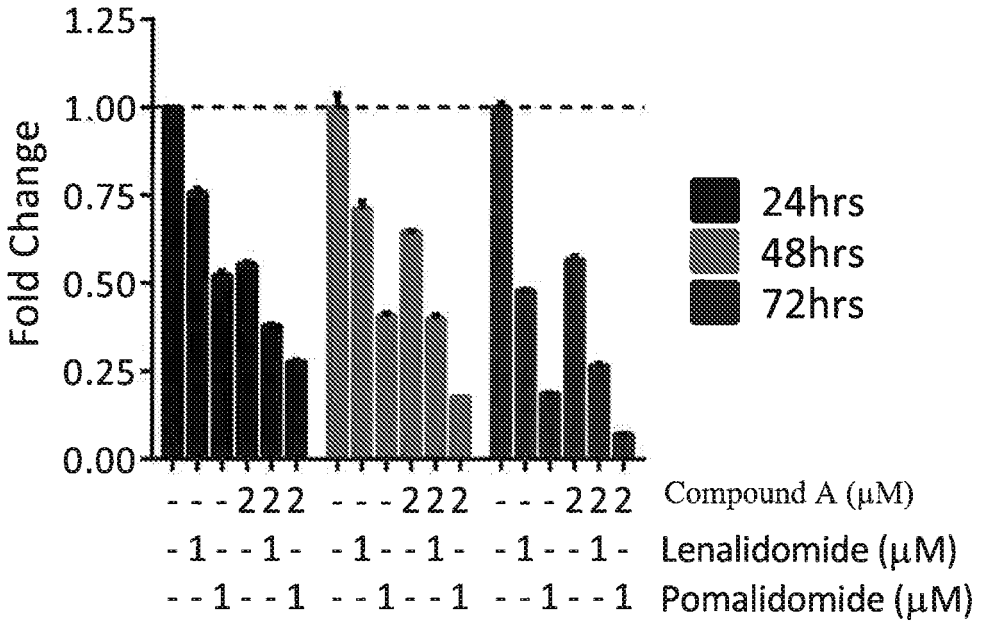
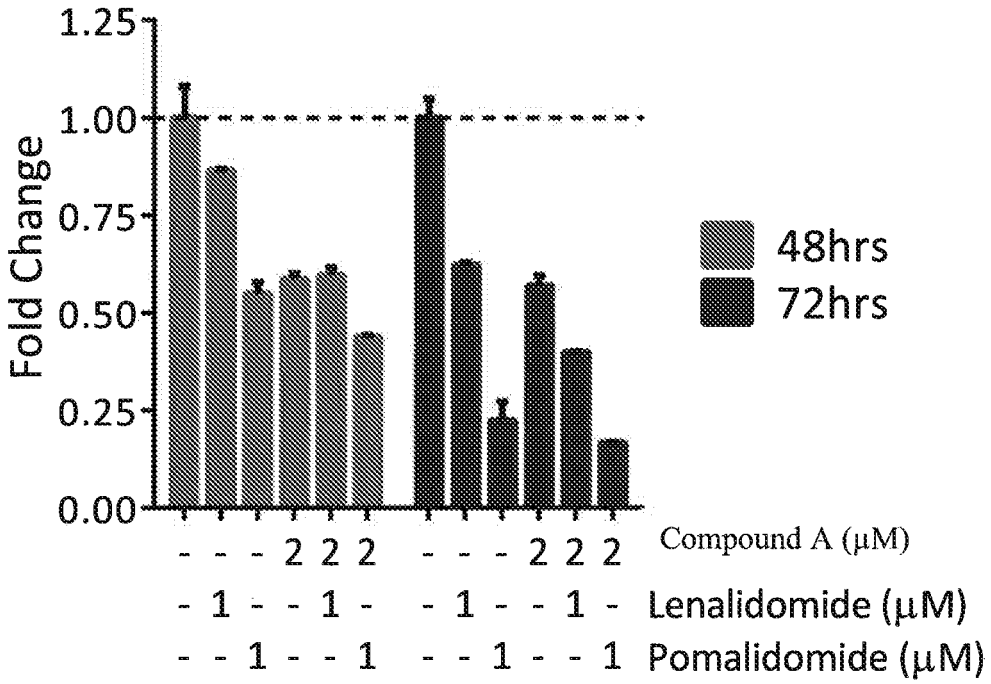

1.25
1.00
0.75
0.50
0.25
0.00
Fold Change
24hrs
48hrs
72hrs
- - - 2 2 2 - - - 2 2 2 - - - 2 2 2 Compound A (μM)
- 1 - - 1 - - 1 - - 1 - - 1 - - 1 - - 1 - Lenalidomide (μM)
- - 1 - - 1 - - 1 - - 1 - - 1 - - 1 - - 1 Pomalidomide (μM)

Figure 12 (cont.)

C



D

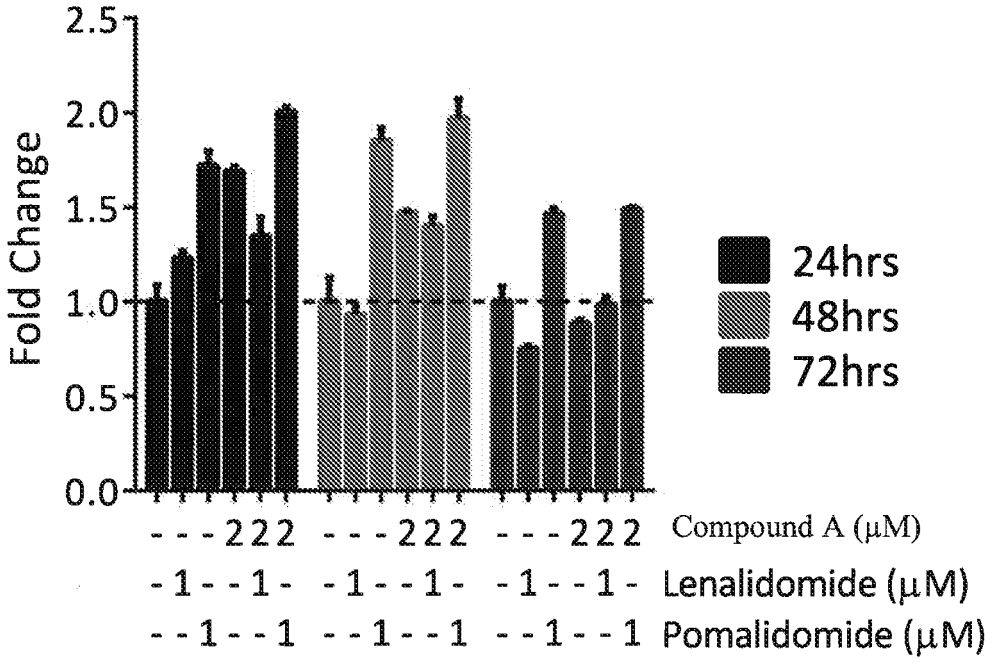
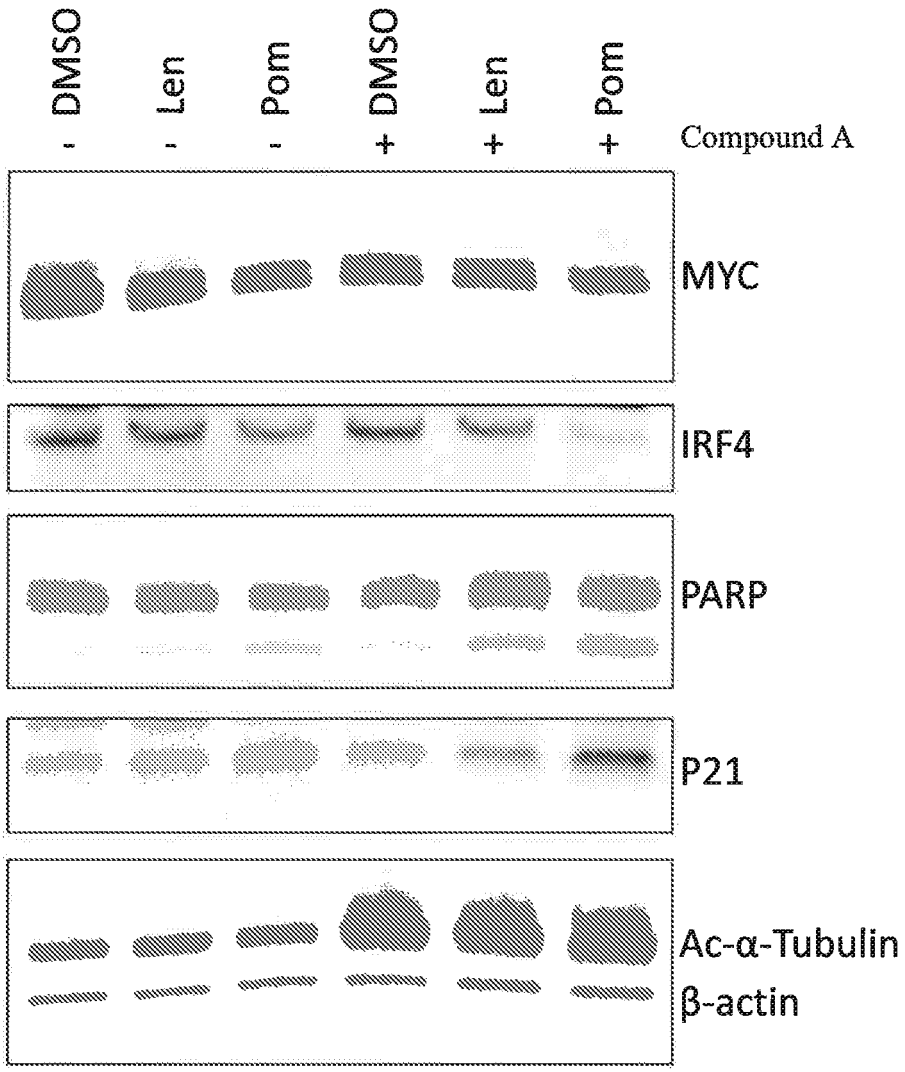


Figure 12 (cont.)

E



F

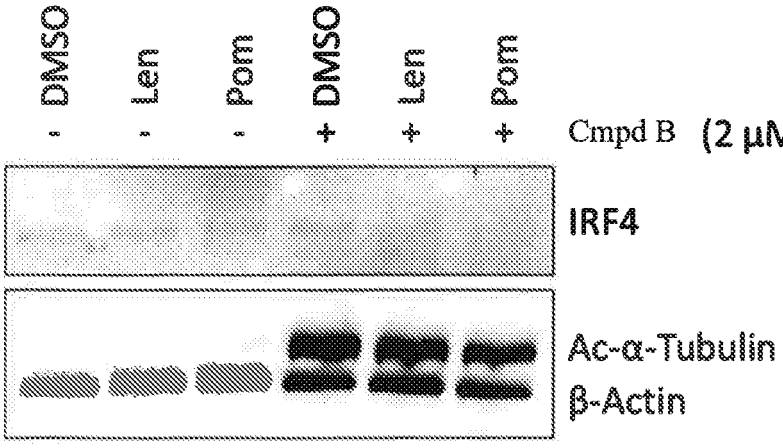
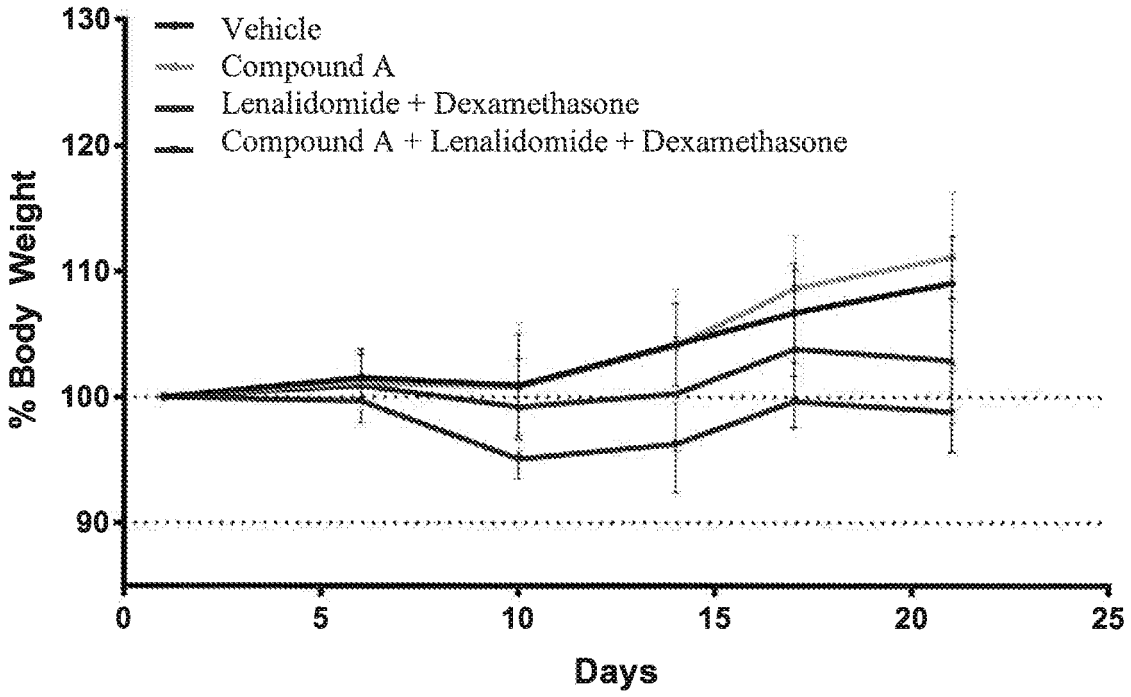
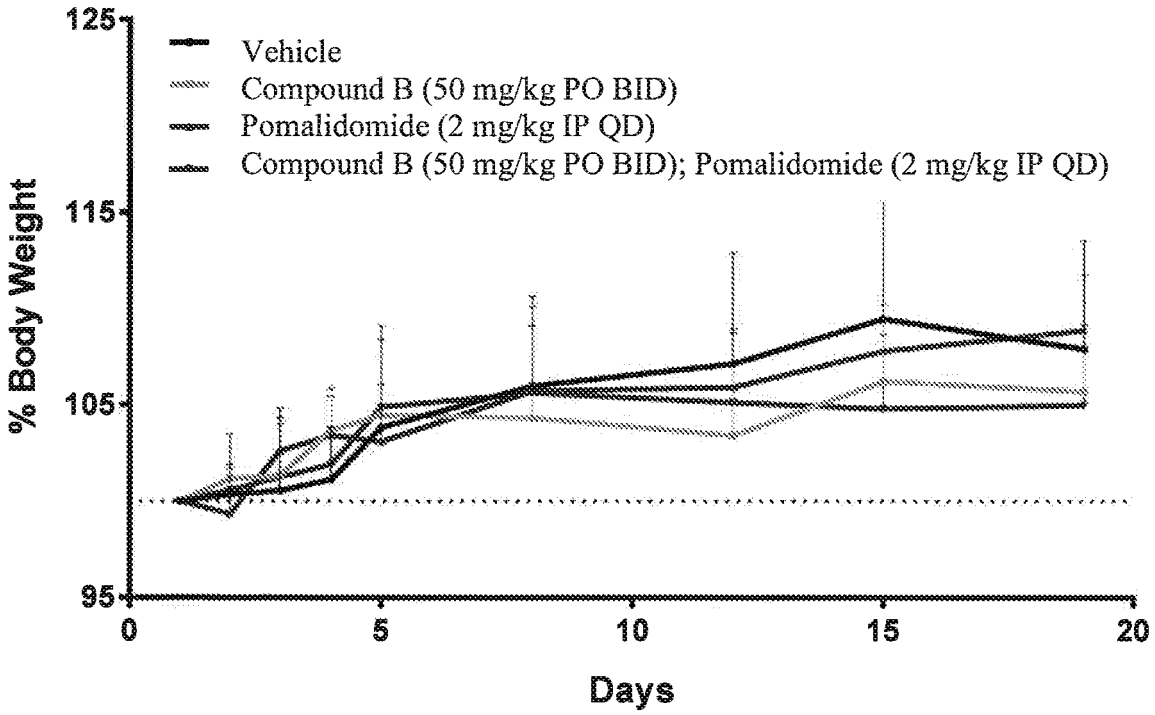


Figure 13

A


Vehicle
Compound A
Lenalidomide + Dexamethasone
Compound A + Lenalidomide + Dexamethasone
% Body Weight
130
120
110
100
90
0
5
10
15
20
25
Days

B


Vehicle
Compound B (50 mg/kg PO BID)
Pomalidomide (2 mg/kg IP QD)
Compound B (50 mg/kg PO BID); Pomalidomide (2 mg/kg IP QD)
% Body Weight
125
115
105
95
0
5
10
15
20
Days